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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/994,576 | 11/27/2001 | Nam Q. Huyn | SURR.79 | 7296 |

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| EXAMINER | |
|---|---|
| LY, CHEYNE D | |
| ART UNIT | PAPER NUMBER |
| 1631 | 8 |

DATE MAILED: 07/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application N . | Applicant(s) | |
|---|---|---|---|
| | 09/994,576 | HUYN, NAM Q. | |
| | Examiner | Art Unit | |
| | Cheyne D Ly | 1631 | |

*-- The MAILING DATE of this communicati n appears on the c ver sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *May 13, 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *11,12,19,23-38 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 13-18, 20-22, 39, 40, and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-42* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 and 5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

1. The art unit designated for this application has changed. Applicants(s) are hereby informed that future correspondence should be directed to Art Unit 1631.

2. Applicant's election without traversal of species A: correlation analysis and E: non-simulated annealing technique, in Paper No. 7, filed May 13, 2003, is acknowledged.

3. Claim 11, 12, 19, 23-38, and 41 have been withdrawn from examination because they are directed to species other than the elected species, correlation analysis and non-simulated annealing technique.

4. Claims 1-10, 13-18, 20-22, 39, 40, and 42 are examined on the merits.

## Information Disclosure Statement

5. Document AAB has not been considered because the cited URL is no longer accessible.

## CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 21 and 22, line 1, the phrase "desired computation time" causes the claims to be vague and indefinite because it is unclear what is being used to the computation time is desirable (CPU time or time generated by a computer). Clarification of the metes and bounds is required.

## *CLAIM REJECTIONS - 35 USC § 102*

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in:
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-7, 13, 16-18, 20-22, 39, 40, and 42 rejected under 35 U.S.C. 102(a) and (e)(2) as being clearly anticipated by Campbell et al. (US 6,059,724 A).

11. Campbell et al. discloses a computer based system (column 9, lines 2-30) and method for predicting the future health of an individual by obtaining longitudinal data for a large number of biomarkers from a large human test population, statistically selecting predictive biomarkers, and determining and assessing an appropriate multivariate evaluation function based upon the selected biomarkers (column 1, lines 8-12). For example, it is known that total serum cholesterol is a biomarker which is related to many diseases (column 10, lines 9-10) for example heart disease is clinically indicated by elevated blood cholesterol (column 3, lines 59-60). The total number of persons in the at risk group, N, is 257,932,000 (column 2, lines 29-36), as in instant claim 13. The method of Campbell et al. comprises analyzing 200 biomarker values from each member of the test population, *n*, (column 15, lines 19-24) and a subset, training sample is selected (column 20, lines 23-27). In the training set, 641 "annual" evaluations, *p*, from 481

subjects and 88 values of Direct Bilirubin, *k*, were available from 80 subjects (column 33, lines 9-14). It is suggested that 200 biomarker values for each member of the test population, *n*, is greater that of 641 evaluations, *p*. Further, 88 values of Direct Bilirubin, *k*, wherein *k* is less than *p*. A list of candidate biomarkers are selected from those listed in Tables 1-5 (column 33, lines 15-41), as in instant claims 1, 39, 40, and 42.

12. As cited above, *n* is 200 biomarker values for each member of the test population of 481 and *p* 641 evaluations; therefore, 10*p* is less than *n*, as in instant claim 4.

13. Further, *k* value of 88 is less 128, which is the value of *p* equal to 641 divided by 5, as in instant claim 5.

14. A subject is classified based on specified biological conditions, as claim 2.

15. The method of Campbell et al. comprises a step for correlation analysis for determining individual's membership in one of two complementary groups of subjects and the explanatory variables are typically biomarkers or functions of biomarkers (column 7, lines 55-67 to column 8, lines 1-9), as in instant claims 3 and 6.

16. The biomarkers values are clustered (column 10, lines 44-53), as in instant claims 7.

17. The biomarkers include all that can be measured in biological samples (column 10, lines 53-56). Further, the said method measures the biomarker values of selected large sets of biomarkers simultaneously (column 15, lines 66-67 to column 17, lines 1-2) as in instant claims 16-18.

18. Campbell et al. discloses estimating quantitatively, for each member of the test population, the probability of acquiring the specified biological condition within the specified

time period or age interval (Abstract etc.) as in instant claims 20-22. (See 112 2nd Paragraph Rejection Section).

**CLAIM REJECTIONS - 35 USC § 103**

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 1-10, 13-18, 20-22, 39, 40, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell et al. (US 6,059,724 A) taken with Eisen et al. (1998) in view of Lucas et al. (US 5,871,946 A).

21. Campbell et al. discloses the limitations of claims 1-7, 13, 16-18, 20-22, 39, 40, and 42 as discussed above.

22. Further, Campbell et al. discloses a method that requires relatively precise calculations of statistical significance (column 23, lines 8-13) and the threshold is set to be between 0 and 1 standard deviation (column 23, lines 60-63).

23. However, Campbell et al. does not disclose the limitations of correlation based on hierarchical cluster, user-selected correlation threshold and ranking of biological markers.

24. Eisen et al. discloses hierarchical cluster analysis is a type of correlation analysis was used for analyzing a large data set (page 14863, column 1, lines 10-15; column 2, lines 3-13; and page 14864, column 1-2, Hierarchical Clustering Section), as in instant claim 8.

25. It is noted that the system of Campbell et al. is directed to a general tool for quantitatively predicting risk, for a selected individual, of a wide range diseases (column 4, lines 39-43), thus, suggesting the said system and method could be used for analyzing any biological marker.

26. Lucas et al. discloses a method of studying biological surface markers (column 42, lines 16-18) and ranking cells by the functional activity of the cell markers (column 33, lines 44-46), as in instant claims 14 and 15.

27. The method of Lucas et al. further comprises a user using a system for inputting numeric values to control the output thresholds (column 49, lines 7-11 and 24-28), as in instant claims 9, 10.

28. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the concept emphasized by Campbell et al. for analyzing a large data set as directed to biomarkers to reliably predict future health problems and improve on the concept by bringing a holistic approach to develop an integrated understanding of a biological system by using hierarchical cluster analysis for analyzing large data sets (column 1, lines 26-30) as taught by Eisen et al. An artisan of ordinary skill in the art would be further motivated to reliably predict future health problems as directed to the biomarkers identified by the method of Lucas et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use a computer system and method for using hierarchical clustering to analyze large data sets such as biological markers to reliably predict future health problems as taught by Campbell et al. taken with Eisen et al. wherein the said system accepts user inputs as taught Lucas et al.

## CONCLUSION

29. NO CLAIM IS ALLOWED.

30. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

32. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

33. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
7/18/03

ARDIN H. MARSCHEL
PRIMARY EXAMINER